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Higher clinical acuity and 7-day hospital mortality in non-COVID-19 acute medical admissions: prospective observational study.

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Abstract

Objectives: To understand the effect of COVID-19 lockdown measures on severity of illness and mortality in non-COVID-19 acute medical admissions.

Design: A prospective observational study

Setting: 3 large acute medical receiving units in NHS Lothian, Scotland.
Participants: Non-COVID-19 acute admissions (n = 1682) were examined over the first 31 days after the implementation of the COVID-19 lockdown policy in the United Kingdom on 23rd March 2019. Patients admitted over a matched interval in the previous 5 years were used as a comparator cohort (n = 14954).

Main outcome measures: Patient demography, biochemical markers of clinical acuity and 7-day hospital inpatient mortality.

Results: Non-COVID-19 acute medical admissions reduced by 44.9% across all 3 sites in comparison to the mean of the preceding 5 years $P < 0.001$. Patients arriving during this period were more likely to be male, of younger age and to arrive by emergency ambulance transport. Non-COVID-19 admissions during lockdown had a greater incidence of acute kidney injury, lactic acidemia and an increased risk of hospital death within 7 days (4.2% vs 2.5%) which persisted after adjustment for confounders (OR 1.87, 95% CI 1.43, 2.41, $P < 0.001$)

Conclusions: These data demonstrate a significant reduction in non-COVID-19 acute medical admissions during the early weeks of lockdown. Patients admitted during this period were of higher clinical acuity with a higher incidence of early inpatient mortality.

Introduction.

COVID-19, the disease manifestation of the SARS-CoV-2 virus global pandemic in 2020 enforced unprecedented change on how the people of the United Kingdom live their lives. From 23rd March 2020 measures were taken to slow the spread of SARS-CoV-2 with the closure of entertainment, hospitality and indoor leisure premises, the advice to stay home and limit all but essential travel and to work from home where at all possible [1].

Self-attendance rates to emergency medicine services sharply declined during this phase, with a marked reduction in patients presenting with a possible myocardial infarction prompting concern that patients with significant acute illness may not be attending hospital for acute medical care [2]. The reasons for this are unclear but may have been due to concerns about being infected with SARS-CoV-2 or burdening the health service during the pandemic. Concerns that this change in healthcare seeking behavior was resulting in public harm were raised following weekly data reports during the first month of lockdown from the National Records of Scotland demonstrating a 79% increase in all-cause mortality for the same week, with 23% of the excess mortality not attributed to COVID-19 [3]. This was supported by data from the Office of National Statistics UK, recording deaths of 22351 for week 16 in 2020 in England and Wales, 11854 more than the five-year average for this week. While COVID-19 is listed on the death certificate in 8758 deaths for this period, this does not represent all of the excess [4].

Community testing for presumed SARS-CoV-2 infection was not adopted in this period. As such it is unclear whether a proportion of this excess mortality results from delayed presentation to health care services with potentially life-threatening conditions unrelated to SARS-CoV-2 infection or due to undiagnosed COVID-19 disease. To investigate this further, we prospectively examined the demography, route of admission, blood markers of medical acuity and adjusted hospital 7-day mortality of non-COVID-19 acute medical admissions to three large acute medical units in a health board in Scotland during the lockdown period. Admissions to the same units over the same time frame in the preceding 5 years were used as comparison.

Study design, setting and participants

We conducted a cohort study using data obtained from Trakcare inpatient management system (Intersystems, Illinois). Patients resident in the NHS Lothian Health Board area who were admitted to the three acute medical units during the 31 day period were examined following the first week of lockdown (23/03/2020). Patients testing positive for SARS-CoV-2 infection were excluded. This was compared with the same 31 day period beginning the same week from the preceding 5 years (13th week of the years 2015 - 2019).

Variables and data sources

The primary outcome was 7-day hospital mortality obtained from Trakcare. Potential confounders included age, sex and socioeconomic deprivation. Age was categorised into 10 year age bands for graphical presentation, and entered as a continuous term into models. Socioeconomic deprivation was represented as quintiles of the Scottish Index of Multiple Deprivation (SIMD) and was obtained from the SIMD database 2020 version published by the Scottish government [5]. Population estimates were obtained from the National Records of Scotland database [6]. Clinical laboratory test results provided measurements for blood lactate, serum creatinine and SARS-CoV-2 test results. Blood lactate was dichotomised at the reference range threshold (≤ 2.4 , > 2.4). Baseline creatinine was obtained on the most recent blood test at least 7 days from hospital admission within the year prior to the patient's admission in order to determine Acute Kidney Injury network (AKIN) score (4 categories: No AKI, Stages 1-3) [7]. This was analysed as a binary variable based on severity of renal injury (no AKI/"Risk":Stage 1 vs "Injury":Stage 2/"Failure":Stage 3). Where baseline creatinine was not available, the median value of the population without known renal impairment was used (69 $\mu\text{mol/l}$). All admitted patients were screened for signs and symptoms of SARS-CoV-2 infection using local guidelines (supplementary material 1) and tested using rtPCR nose and throat combined swab where criteria are met. If this was negative and clinical suspicion persisted a second swab was performed. Any patients testing positive at any stage during admission were removed from the study.

Statistical methods

Analyses were undertaken using R version 3.6.1. Graphical outputs were performed using ggplot2 package. Missing data for renal biochemistry and lactate were included in the analysis as being 'no AKI' or $\leq 2.4 \text{ mmol/l}$ as consultation with clinicians indicated that these tests were considerably more likely to be omitted where there is clinically no indication to perform the test. Baseline characteristics and mode of admission were compared between lockdown and pre-lockdown cohorts using Mann-Whitney U or chi-squared tests as indicated. Admission rate and 7 day hospital mortality per head of population were calculated using the number of admissions of events per head of population for the region for the lockdown period relative to the mean of the previous 5 years and P value determined using Poisson regression. 7-day hospital mortality, severity of acute kidney injury and lactic acidemia on admission was compared for the admitted population in the lockdown period relative to previous years using binary logistic regression and adjusted for age, sex and deprivation. To evaluate the robustness of the missingness mechanism for acute kidney injury and lactic acidemia (Not

Missing at Random assumption), we conducted a complete case analysis for the association between lockdown period and these two variables in sensitivity analyses. The project was reviewed by NHS Lothian Research and Development department and Caldicott and deemed not to require ethical approval. The project was undertaken in line with local information governance procedures.

Results.

1682 non-COVID-19 medical admissions were identified during the 2020 lockdown period and compared to 14954 acute medical admissions from a matched period in the previous 5 years. Non-COVID-19 admissions to acute medical units fell by 44.9% in comparison to the mean of the preceding 5 years ($P < 0.001$, figure 1). Numerical data for demographics, source of referral, incidence of AKI, lactic acidemia and 7 day mortality during the lockdown period and compared to the previous 5 years are demonstrated in table 1. Patients admitted during the lockdown period were younger (median 69 vs 72, IQR 26, $p < 0.001$) (figure 2) more likely to be male (49.5% vs 45.5% $P < 0.001$), and more likely to arrive by emergency ambulance than other modes of attendance (53% vs 37.7%, $P < 0.001$). When examining acuity of illness, there was a small but significant increase in patients with AKI (6.7% vs 4.7%) and lactic acidemia (12.4% vs 7.3%) which persisted after adjustment for confounders (AKI = OR 1.44, 95% CI 1.17, 1.77, $P < 0.001$, lactic acidemia = OR 1.79, 95% CI 1.52, 2.09, $P < 0.001$). In sensitivity analyses using a complete case approach to assess the impact of missing values, the lockdown period was still associated with a higher incidence of AKI (OR 1.42, 85%CI 1.15, 1.73, $P < 0.01$), but did not reach significance for lactic acidemia (OR 1.18, 95% CI 0.99, 1.40, $P = 0.05$). Patients admitted to acute medical units during the COVID-19 lockdown period had over twice the risk of death within 7 days of admission when compared to the previous 5 years (4.2% vs 2.5%) which persisted after adjustment for confounders (OR 1.87, 95% CI 1.43, 2.41, $P < 0.001$) (figure 3). However, there was no increase in the absolute rate of patients dying 7 days following acute medical admission as a proportion of the population as a whole (8.43 vs 7.82 per 100,000 population, $P = 0.57$) (Figure 4).

Discussion.

These data suggest that admissions to acute medical units fell considerably during the initial national lockdown phase of the pandemic. We have demonstrated that patients admitted to AMUs were younger, more likely to be male and were clinically more unwell with more severe

renal injury, greater incidence of lactic acidemia and a significantly higher incidence of in-hospital 7-day mortality.

There are several possible explanations for these findings. The younger demographic could be due to more elderly patients being preferentially managed at home to avoid COVID exposure. This may have been driven by patient preference, primary care physician recommendation or the increased availability of family members to provide support at home. The increase in attendance by emergency ambulance suggests an increase in patient acuity however it may also reflect a change in patient behaviour in accessing healthcare during periods that general practices were performing patient care remotely by telephone appointment.

Late presentation with time sensitive pathologies such as sepsis, stroke or myocardial infarction worsens outcome [8–10]. It is possible that the higher level of illness acuity and higher mortality is due to this phenomenon.

Alternatively, it was observed that although the incidence of death was higher in the admission cohort during lockdown, this cohort was smaller than a similar time frame for previous years and therefore a smaller denominator. The rate of 7-day mortality following acute medical admission was unchanged as a proportion of the whole population and it is possible therefore that the observed increase in risk of death is due to fewer less unwell patients being admitted. What is not known is the clinical outcome of patients who did not attend during this period who may have done so in previous years. A more detailed understanding of the rate and cause of non-COVID-19 related community deaths during this period may clarify this point.

This study includes patients with either a lack of signs or symptoms of SARS-CoV-2 infection and those with features of COVID-19 in whom laboratory swab results were negative. The nose and throat swab test for SARS-CoV-2 is widely reported to have sensitivity limitations possibly due predominance of the infection in the lungs with relatively little in the upper respiratory tract [11]. Locally we have found that 18% of patients admitted to hospital testing positive for SARS-CoV-2 were diagnosed on a subsequent follow up swab (unpublished data). Local guidelines which require repeat testing in those with a high clinical suspicion of COVID-19 may ameliorate this effect. Furthermore, patients with COVID-19 can present with atypical symptoms and signs, such as rash, seizures and gastrointestinal haemorrhage or stroke, which would not trigger testing under our local guidelines [12–14]. It may be therefore that a proportion of the increase in patient acuity and death observed is due to undiagnosed SARS-CoV-2 infection. The expansion of testing to include all hospital admissions in future may help to clarify this.

This study adds to the current literature on non-COVID-19 related healthcare contacts during the pandemic. Previous reports demonstrate active healthcare avoidance with a reduction in paediatric emergency care attendance with minor illnesses and more concerning, evidence of delayed presentation of new onset type 1 diabetes with diabetic ketoacidosis and acute myocardial infarction [15–18]. Riley and colleagues describe a reduction in unselected acute medical admission numbers and a change in pathology case mix but no increase in non-COVID-19 related inpatient mortality in comparison to the previous year [19]. We build on this work by analysing admission rates adjusted for regional population size, serum markers of clinical acuity and by extending to the previous 5 years to account for annual variation. In addition, our study reports mortality rates adjusted for age, sex and deprivation quintile which may account for the difference in findings.

There are limitations to this study. For expediency of reporting, disease coding and stratification of presenting pathology is not available at the time of writing and future analysis of case-mix and cause of death in this cohort may allow more detailed understanding of these findings. During the lockdown period, a higher proportion of patients with time-sensitive pathologies such as severe sepsis, myocardial infarction and stroke may bypass acute medical units and be directed to specialist units or critical care units. Furthermore, a higher proportion of patients may die in the community with similar pathologies. However, exclusion of these groups from the study population would bias our mortality findings towards the null.

Conclusion.

The COVID-19 pandemic has been associated with a significant reduction in acute medical admissions. However, those attending are younger with greater medical acuity and a higher risk of inpatient mortality. Ongoing public health efforts must be made to ensure patients seek medical attention appropriately in the context of acute medical illness during pandemic lockdown periods.

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Summary Box

What is already known:

The effect of social distancing measures on non-COVID-19 related acute medical admissions and outcomes remains incompletely described. Previous studies suggest a reduction in emergency department attendance and acute medical admission rates. Delayed presentation of specific time sensitive pathologies such as myocardial infarction and diabetic ketoacidosis have also been reported.

What this study adds:

This single centre study in three acute medical units builds on published data and describes the effect of COVID-19 lockdown on the demography, admission rate and clinical acuity of patients admitted to acute medical services in a large healthcare trust in Lothian, UK. Social distancing measures were associated with a reduction in non-COVID-19 related admissions. Admitted patients were younger, more likely be male and demonstrated a higher level of clinical acuity as measured by a higher incidence of renal injury, lactic acidaemia and early inpatient mortality.

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Contributors

Dr Marcus Lyall (Guarantor): Design of study, data collection and linkage, statistical analysis, manuscript preparation. Dr Nazir Lone: Study design, statistical analysis, and manuscript preparation.

Data Sharing Statement

Subject to appropriate NHS Lothian governance approval we invite groups to submit requests for data sharing for the purposes of research and confirmatory analysis.

Role of the funding source

ML is supported by an NHS research Scotland Clinical Fellowship. NL declares no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. This project was conducted without influence from the respective funding bodies.

Ethics Approval

The study was reviewed by the Quality Improvement Team and registered in NHS Lothian as a Quality Improvement project. Following the HRA decision tool and after seeking advice from NHS Lothian Research and Development department, the study was deemed to be service evaluation and therefore formal ethical approval was not required. All data were anonymised before analysis and complied with local data protection requirements.

PPI statement

We did not directly include PPI in this study, but the database used in the study was developed with PPI and is updated by a committee that includes patient representatives.

Figure Legends

Figure 1) Rate of admission to the acute medical units of three hospitals in Lothian with total rate for the region. (* = $P < 0.001$ Poisson regression analysis, COVID-19 lockdown versus previous years)

Figure 2) Age composition of acute medical admission cohorts for COVID-19 lockdown versus mean of previous 5 years (blue). * $P < 0.001$ Mann–Whitney U Test.

Figure 3) Binary logistic regression modelling of age, sex and SIMD adjusted 7-day hospital mortality of non-COVID-19 admissions ($n = 1682$) versus 5 previous years ($n = 14954$). Dashed lines = 95%CI.

Figure 4) Rate of 7-day hospital deaths following acute medical admission as a function of total population during COVID-19 lockdown (red) versus previous 5 years (blue) with previous 5 year mean (dotted line).

| | pre-lockdown n = 14954 | COVID-19 lockdown n = 1682 | |
|----------------------------------|---------------------------|-------------------------------|------------------------|
| male sex - no. (%) | 6803 (45.5) | 832 (49.5) | P < 0.01* |
| age median(IQR) | 72 (26) | 69 (26) | P < 0.001 [§] |
| emergency ambulance - no. (%) | 5633 (37.7) | 892(53) | P < 0.001* |
| SIMD quintile - no.(%) | | | P = 0.09 |
| 1 | 2504 (16.7) | 305 (18.1) | |
| 2 | 4205 (28.1) | 441 (26.2) | |
| 3 | 2650 (17.7) | 278 (16.5) | |
| 4 | 2230 (14.9) | 280 (16.6) | |
| 5 | 3357 (22.4) | 377 (22.4) | |
| AKIN score 0-1 - no. (%) | 14292 (95.6) | 1578 (93.8) | P < 0.001 [†] |
| AKIN score 2-3 - no. (%) | 662 (4.4) | 104 (6.2) | |
| Lactate - no. (%) | | | P < 0.001 [†] |
| lactate ≤2.4mmol/l | 13864 (92.7) | 1473 (87.6) | |
| lactate > 2.4mmol/l | 1090 (7.3) | 209 (12.4) | |
| 7 day inpatient mortality | 374 (2.5) | 71 (4.2) | P < 0.001 [†] |

Table 1) Demographics, mode of arrival, incidence of acute kidney injury, lactic acidemia and 7-day inpatient mortality in acute medical admissions during the first 5 weeks of lockdown in comparison to previous years. Missing values for SIMD quintile: pre-lockdown 8 (0.1%); COVID-19 lockdown 1 (0.1%). Missing values for AKI (pre-lockdown 510 (3.4%), COVID-19 lockdown 38 (2.3%) and lactate (pre-lockdown 9782 (65.4%), COVID-19 lockdown 812 (48.3%) were combined with the AKIN score 0-1 group and lactate ≤2.4mmol/l respectively as described in methods. * = Chi-squared analysis, [§] = Mann-Whitney u test, [†] = binary logistic regression.